

Editorial

Vitrectomy for diabetic macular edema; where are we?



Diabetic retinopathy is the leading cause of visual impairment in the working age group mainly due to diabetic macular edema (DME).^{1,2}

As the incidence of diabetes is increasing in human populations, the visual burden of DME is expected to expand. The standard treatment for DME has been macular laser photocoagulation³ for almost two decades but has shifted to intravitreal injection of anti-VEGF agents over the past decade. Although the intravitreal injection of these drugs and even steroids has been shown to be superior to macular laser photocoagulation,^{4–10} there is much to be desired in the treatment of DME.

It has been suggested that attached vitreous may have an adverse effect on the clinical course of DME. Posterior vitreous detachment has been reported to be less common in eyes with DME and that attached vitreous may diminish the benefit of intravitreal steroid therapy.¹¹ On this basis, some authors have suggested pars plana vitrectomy and removal of posterior hyaloid with or without ILM removal for treatment of DME.

The DRCR network has reported the results of vitrectomy in cases of vitreomacular traction associated with diabetic retinopathy.¹² The macular thickness significantly decreased in most eyes. Between 28% and 49% of eyes experienced improvement of visual acuity, whereas in 13%–31% the visual acuity worsened. In patients without vitreomacular traction, with or without epiretinal membranes, however, the results of vitrectomy have been more variable and the majority of studies have reported non-significant visual improvement despite initial structural improvement. Simunovic et al¹³ published a systematic review and meta-analysis on the outcomes of vitrectomy for DME and concluded that there is little evidence to support vitrectomy as a treatment for diabetic macular edema in the absence of epiretinal membrane or vitreomacular traction and that although vitrectomy appears to be superior to laser in its effects on retinal structure at 6 months, no such benefit has been proven at 12 months. Similar results were obtained by Jackson et al¹⁴ in their recent systematic review, meta-analysis, and synthesis of safety literature. They did not identify any major safety concerns.

In this issue, Ghassemi et al have studied a group of 12 eyes with non-tractional epiretinal membranes associated with

DME refractory to at least 2 intravitreal injections of bevacizumab and one injection of triamcinolone acetonide. Vitrectomy, membranectomy, and ILM peeling was performed in these patients which resulted in significant reduction of central macular thickness without a parallel significant improvement in visual acuity. These results are well based in literature as mentioned previously. The authors are to be commended for their study of the subgroup of eyes with non-tractional epiretinal membranes specifically, which has not been clearly reported in literature.

Despite these findings, the role of vitrectomy in the treatment of DME without vitreomacular traction cannot be entirely ruled out. It should be considered that in many cases reported in literature, including the cases studied by Ghassemi et al, vitrectomy has been performed on eyes with long-standing macular edema. It is conceivable that such eyes have already sustained marked structural damage which makes them refractory to any kind of treatment including vitrectomy. In other words, these eyes may be refractory to vitrectomy for the very reason that they are refractory to anti-VEGF agents. It is quite likely that vitrectomy and its resultant decrease in macular edema would lead to vision improvement in eyes without much structural damage. In fact, two studies have already demonstrated a correlation between the pre-vitrectomy integrity of outer retina (external limiting membrane and ellipsoid zone) and the potential for vision improvement after vitrectomy.^{15,16} Adequately sized randomized clinical trial are needed to elucidate the role of vitrectomy on the amount and duration of visual improvement in eyes with preserved outer retina as compared to other treatment modalities.

References

1. Kempen JH, O'Colmain BJ, Leske MC, et al. The prevalence of diabetic retinopathy among adults in the United States. *Arch Ophthalmol*. 2004;122:552–563.
2. Congdon NG, Friedman DS, Lietman T. Important causes of visual impairment in the world today. *JAMA*. 2003;290:2057–2060.
3. Photocoagulation for diabetic macular edema. Early treatment diabetic retinopathy study report number 1. Early treatment diabetic retinopathy study research group. *Arch Ophthalmol*. 1985;103:1796–1806.
4. Haller JA, Kuppermann BD, Blumenkranz MS, et al. Randomized controlled trial of an intravitreal dexamethasone drug delivery system in patients with diabetic macular edema. *Arch Ophthalmol*. 2010;128:289–296.

Peer review under responsibility of the Iranian Society of Ophthalmology.

5. Gillies MC, Sutter FK, Simpson JM, et al. Intravitreal triamcinolone for refractory diabetic macular edema: two-year results of a double-masked, placebo-controlled, randomized clinical trial. *Ophthalmology*. 2006;113:1533–1538.
6. Sutter FK, Simpson JM, Gillies MC. Intravitreal triamcinolone for diabetic macular edema that persists after laser treatment: three-month efficacy and safety results of a prospective, randomized, double-masked, placebo-controlled clinical trial. *Ophthalmology*. 2004;111:2044–2049.
7. Kuppermann BD, Blumenkranz MS, Haller JA, et al. Randomized controlled study of an intravitreal dexamethasone drug delivery system in patients with persistent macular edema. *Arch Ophthalmol*. 2007;125:309–317.
8. Massin P, Audren F, Haouchine B, et al. Intravitreal triamcinolone acetonide for diabetic diffuse macular edema: preliminary results of a prospective controlled trial. *Ophthalmology*. 2004;111:218–224. discussion 224–215.
9. Aiello LP, Avery RL, Arrigg PG, et al. Vascular endothelial growth factor in ocular fluid of patients with diabetic retinopathy and other retinal disorders. *N Engl J Med*. 1994;331:1480–1487.
10. Grant MB, Afzal A, Spoerri P, et al. The role of growth factors in the pathogenesis of diabetic retinopathy. *Expert Opin Inv Drug*. 2004;13:1275–1293.
11. Sivaprasad S, Ockrim Z, Massadoutis P, et al. Posterior hyaloid changes following intravitreal triamcinolone and macular laser for diffuse diabetic macular edema. *Retina*. 2008;28:1435–1442.
12. Diabetic Retinopathy Clinical Research Network Writing Committee, Haller JA, Qin H, Apte RS, et al. Vitrectomy outcomes in eyes with diabetic macular edema and vitreomacular traction. *Ophthalmology*. 2010;117(6):1087–1093.
13. Simunovic MP, Hunyor AP, Ho IV. Vitrectomy for diabetic macular edema: a systematic review and meta-analysis. *Can J Ophthalmol*. 2014 Apr;49(2):188–195.
14. Jackson TL, Nicod E, Angelis A, Grimaldi F, Pringle E, Kanavos P. Pars plana vitrectomy for diabetic macular edema: a systematic review, meta-analysis, and synthesis of safety literature. *RETINA*. 2016;0:1–10.
15. Chhablani JK, Kim JS, Cheng L, Kozak I, Freeman W. External limiting membrane as a predictor of visual improvement in diabetic macular edema after pars plana vitrectomy. *Graefes Arch Clin Exp Ophthalmol*. 2012;250:1415–1420.
16. Hirano T, Murata T. Vitrectomy for DME without macular traction. *Retina Physician*. 2013;10(6):6164.

Mehdi Modarres, MD

Eye Research Center, Iran University of Medical Sciences,
Tehran, Iran